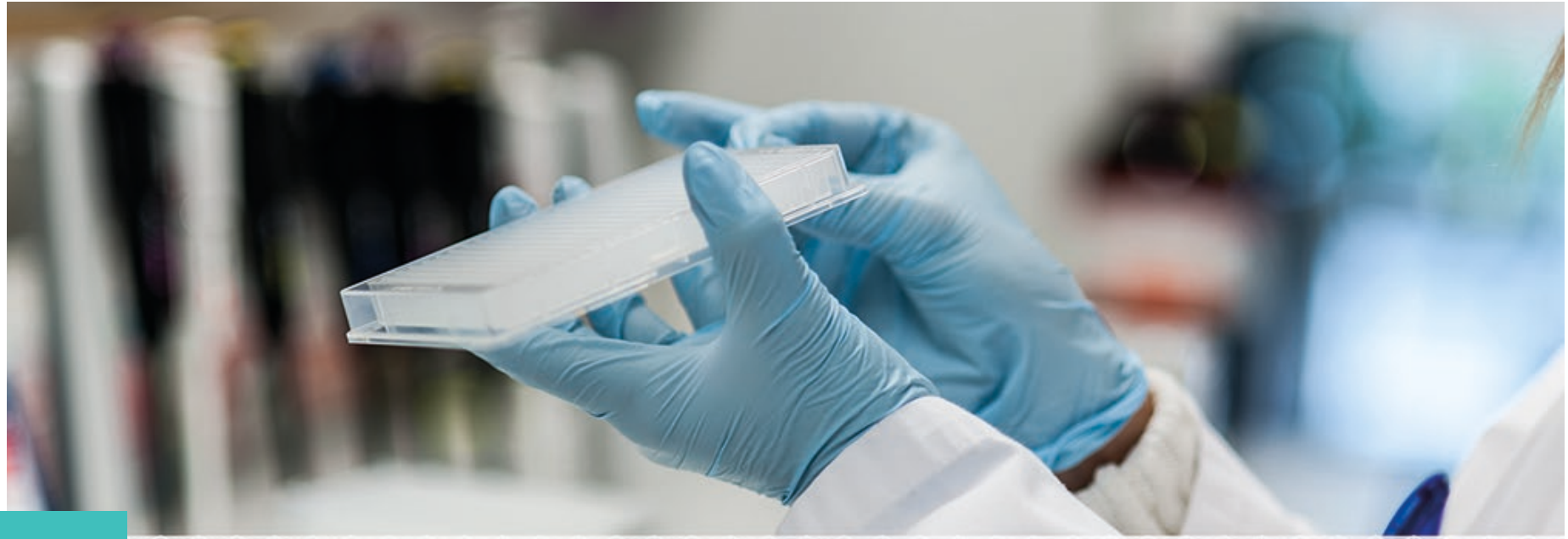


Introduction to EATRIS ERIC

European Infrastructure for Translational Medicine

March 7th, 2019
Sofia, Bulgaria

ESFRI European Research Infrastructure

- Facilities, resources and services used by the research communities to **conduct research** and **foster innovation** in their fields.

- **Major scientific equipment** (or sets of instruments), **knowledge-based resources** such as collections, archives and scientific data, e-infrastructures

European Research Infrastructure Consortium (ERIC)

- A European joint-venture (also allows the participation of non-European countries)
- A legal capacity recognised in all EU Member States
- Flexibility to adapt to specific requirements of each infrastructure
- Part of wider ESFRI community
- Exemptions from VAT and excise duty

EATRIS is an ERIC since Jan 2014

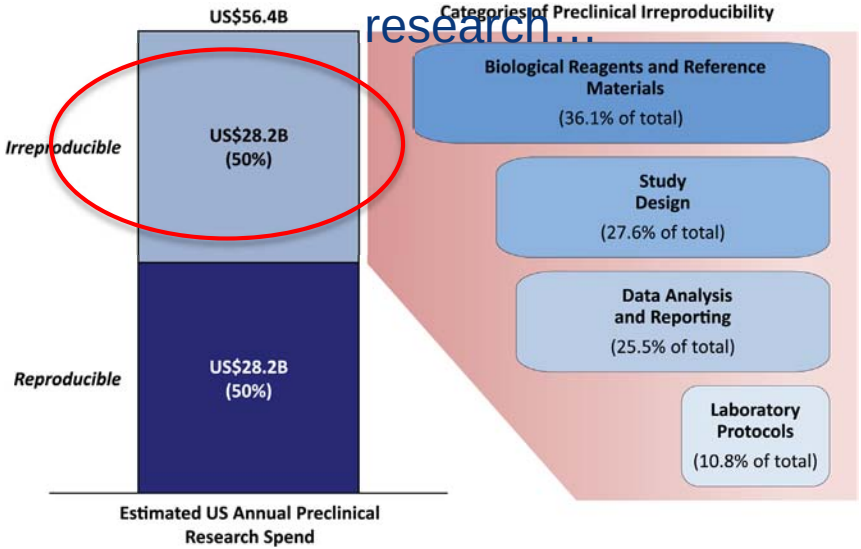
https://ec.europa.eu/research/infrastructures/index.cfm?pg=eric

RI role in Europe

- High quality – state of the art facilities and resources across Member States
- Professional **access and services** (to researchers)
- **Capacity utilization** (EU-wide long term planning)
- Mandate to tackle systemic issues such as:
  - **Reproducibility**
  - **Standardisation and harmonization**
  - Improving our ability to generate knowledge & innovation

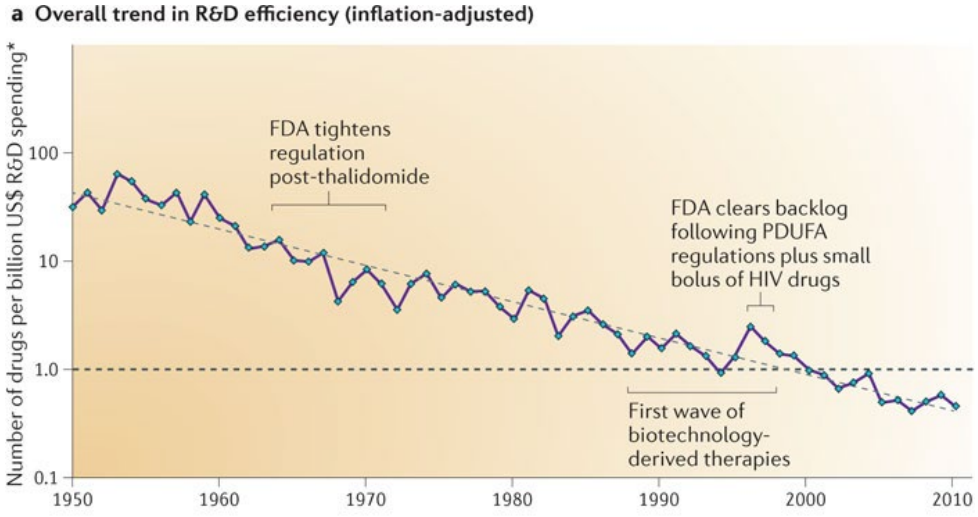
Broken biomedical innovation pipeline

Spending on non-reproducible research…



Freedman et al PLOS Biology (2015)

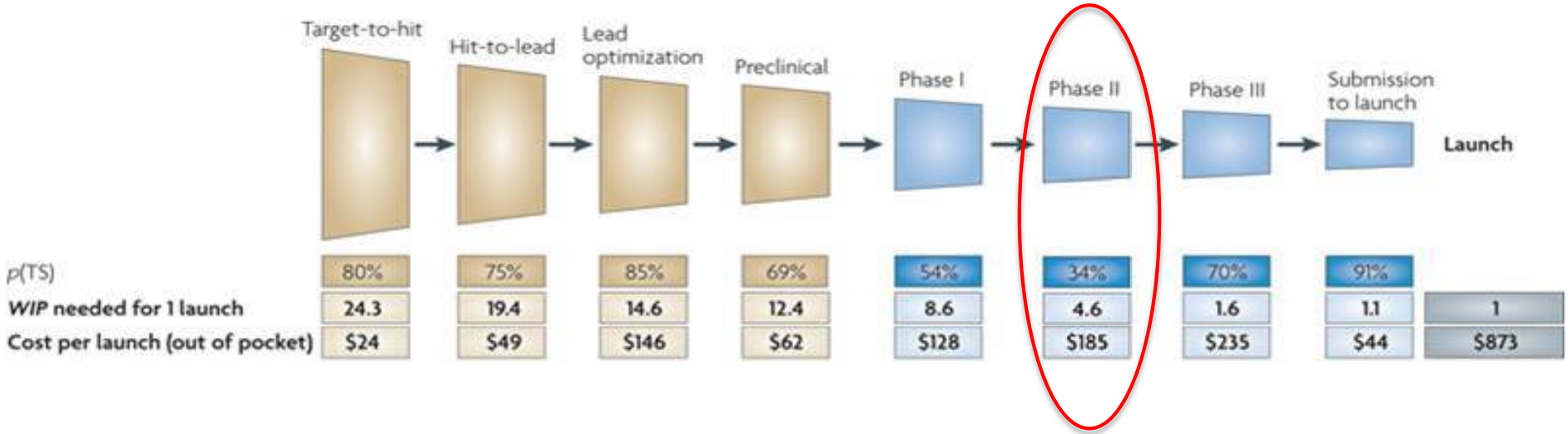
…Feeds a declining pipeline



Scannell et al Nat Rev Drug Disc (2012)

Failing too late in development

Ca. 65% fail at phase II



Adapted from Paul et al; Nat Rev Drug Disc (2010)

Translational Medicine

Right target

- Strong link between target and disease
- Differentiated efficacy
- Available and predictive biomarkers

Right tissue

- Adequate bioavailability and tissue exposure
- Definition of PD biomarkers
- Clear understanding of preclinical and clinical PK/PD
- Understanding of drug–drug interactions

Right safety

- Differentiated and clear safety margins
- Understanding of secondary pharmacology risk
- Understanding of reactive metabolites, genotoxicity and drug–drug interactions
- Understanding of target liability

Right patient

- Identification of the most responsive patient population
- Definition of risk–benefit for a given population

Right commercial potential

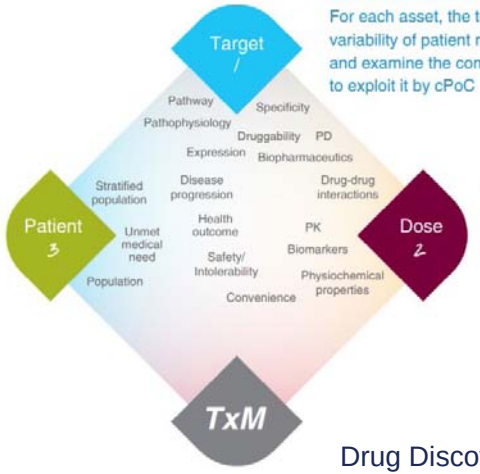
- Differentiated value proposition versus future standard of care
- Focus on market access, payer and provider
- Personalized health-care strategy, including diagnostics and biomarkers

Figure 1 | **The 5R framework.** Summary of the key features of the five-dimensional framework: the right target, right tissue, right safety, right patient and right commercial potential. PD, pharmacodynamic; PK, pharmacokinetic.

Nat. Rev. Drug Discovery 2018

Right biological target for the selected disease
For each asset, the team must quantify variability of patient response (efficacy) and examine the commercial approach to exploit it by cPoC

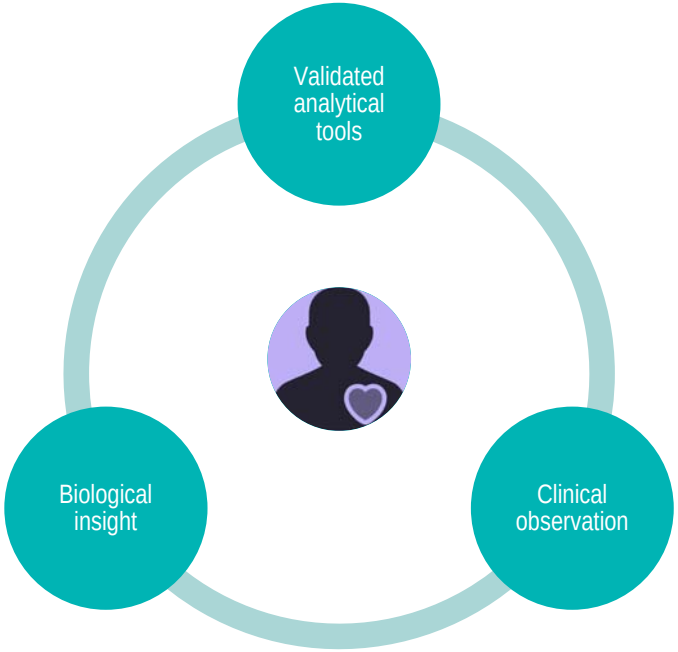
Right patient group in the selected disease
If stratification is appropriate for a given program, stratification strategy and companion diagnostics will need to be validated before initiating Phase III



Right therapeutic window
Dose, regimen, and molecule are optimal at the end of cPoC

Drug Discovery Today 2016

Bench to bedside and back



For early decision-making

To perform translational research

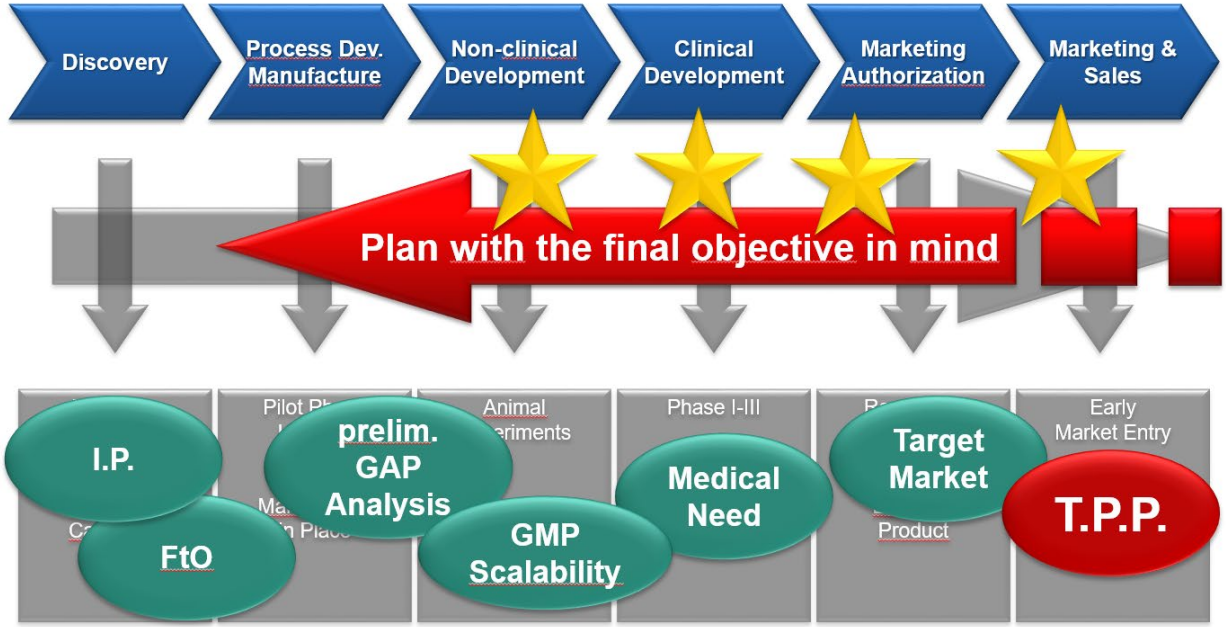
- Create multi-disciplinary teams per project requirements
- Bring together deep understanding of the biology and the clinical presentation
- Use latest - validated - analytical technologies

For a better mechanistic understanding of the disease and potential therapeutic

Translational research in academia

- From deep, intra-disciplinary exploration to **multi-disciplinary**, confirmatory research
- From open question to **goal orientation**
- Many factors beyond the scientific concept dictate success:
  - Creating a product that fits the **clinical** workflow
  - Convincing **industry** that the product represents value
  - Convincing the **regulators** that the product is safe and efficacious
  - Convincing the **payors** that the product is cost-effective
  - Convincing **doctors** that the product addresses the medical need

The path to the patient – in a reverse approach



EATRIS Positioning

Vision

Making translation of scientific discoveries into medical products more effective to improve human health and quality of life.

Mission

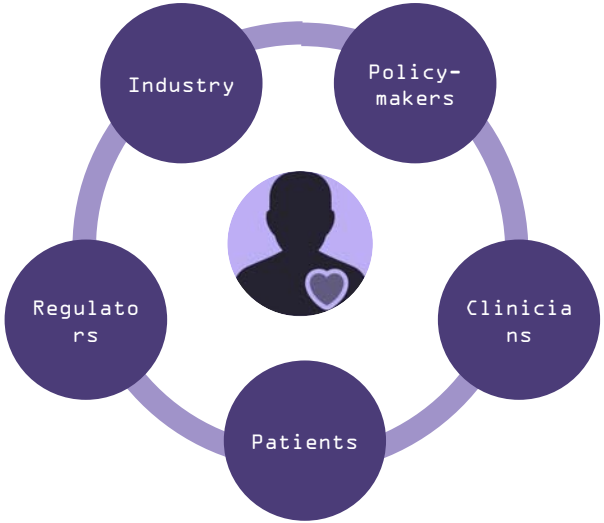
To support researchers in developing their biomedical discoveries into **novel translational tools and interventions** for better health outcomes for society.

Supporting academia, industry, patients and policy makers

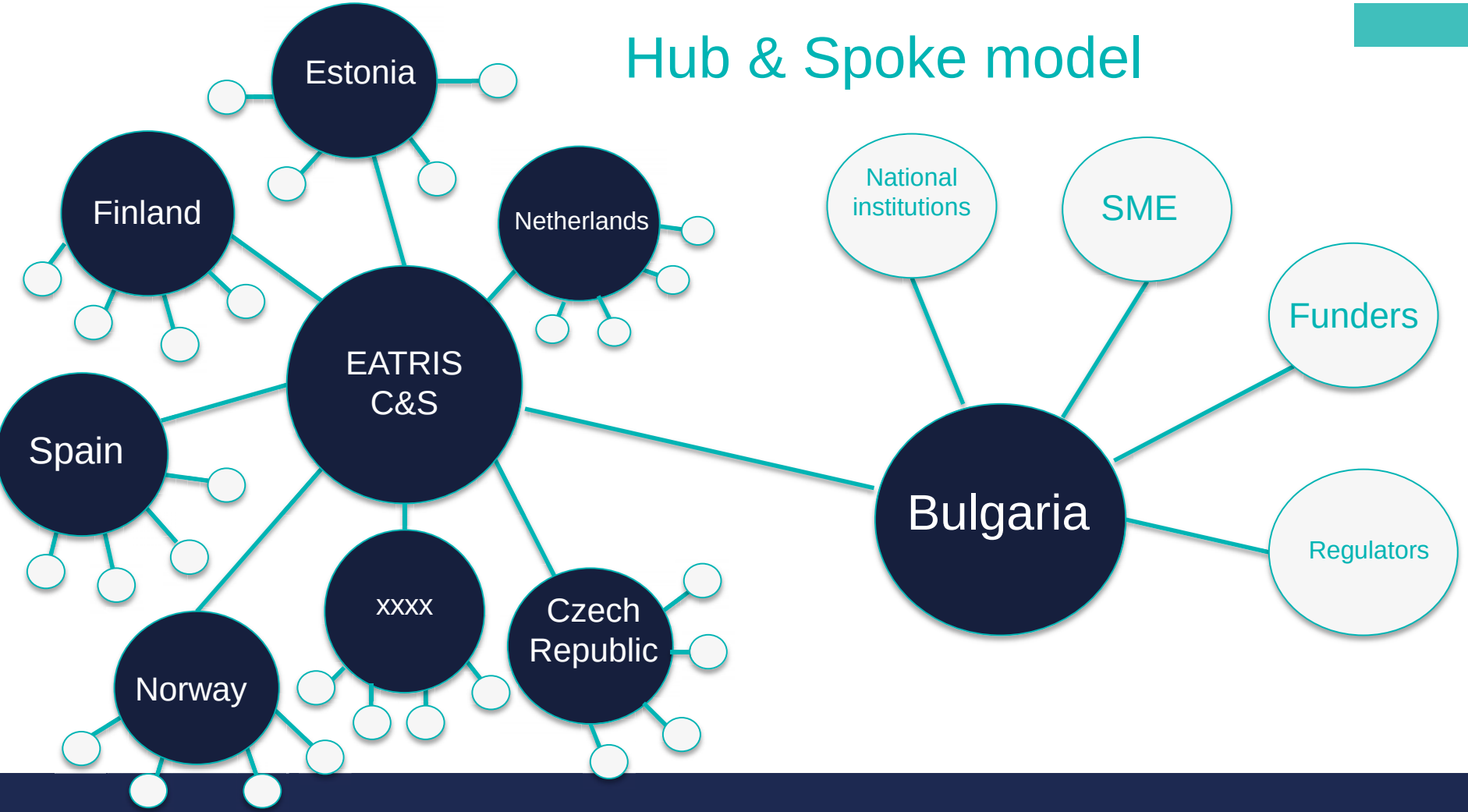
EATRIS approach

We make the translational community accessible to researchers

- Access to quality **research infrastructure services**
- Support **multi-disciplinary, patient-oriented** research
- Ensure **optimal methodological approach**, best infrastructure & resources
- Easy access to **industry, regulatory expertise**



Hub & Spoke model

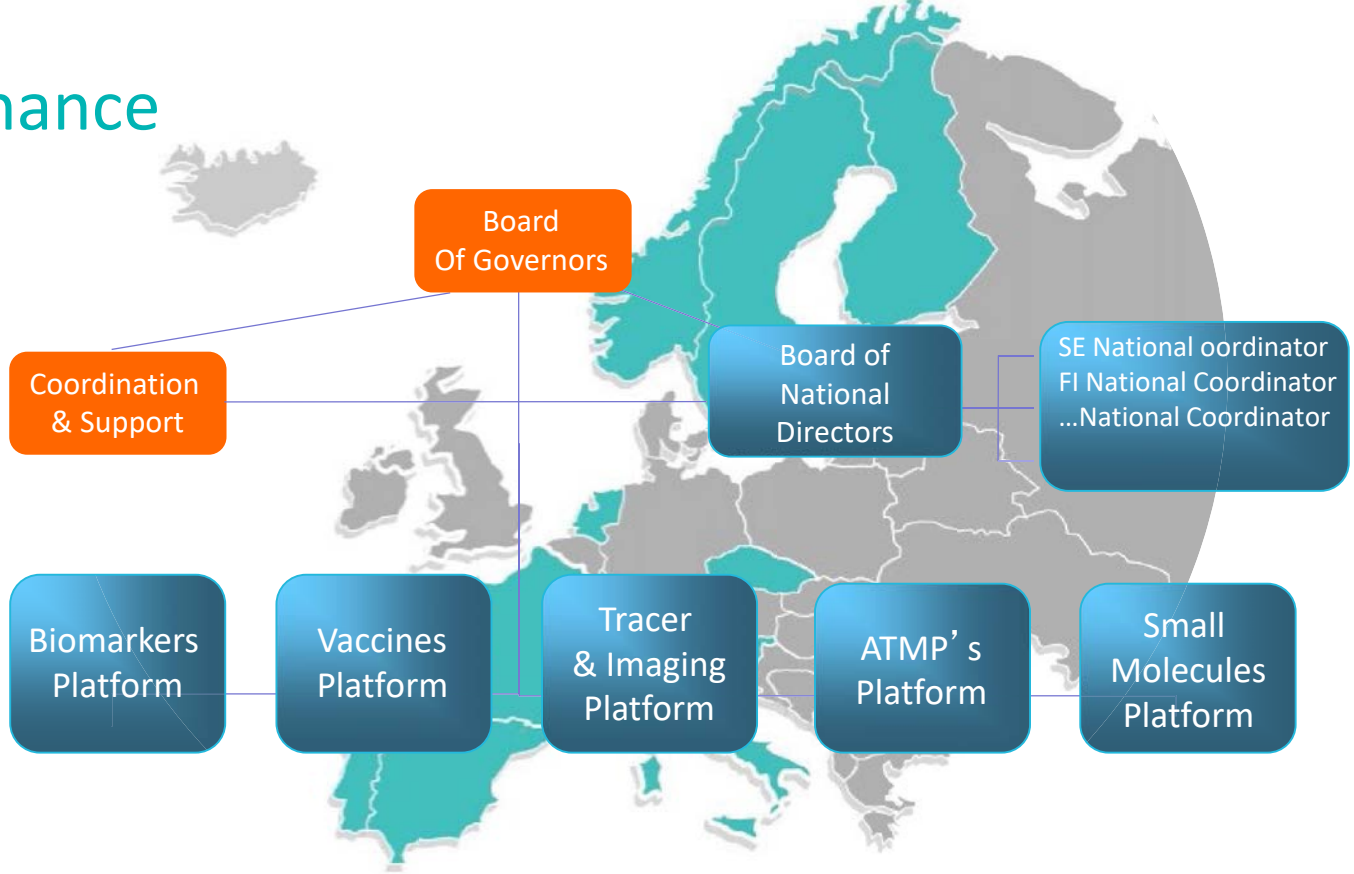


Strategic Goals 2019-2022

Governance

Coordination & strategy

Content, Quality & Execution



90 research institutions of excellence in translational medicine

Coordination & Support Team















Amsterdam

NL


EATRIS Product Platforms

Imaging & Tracing

Cyril Poupon
Neurospin
Paris, FR

Bert Windhorst
VU Medical Center
Amsterdam, NL

→ *34 institutions, (8 countries)*

ATMP & Biologicals

Maria Cristina Galli
ISS, IT

Miguel Chillon
VHIR, ES

→ *38 institutions, (9 countries)*

Biomarkers

Alain van Gool
Radboudumc,
TNO, NL

Laura Bermejo
IRYCIS, ES

Andreas Scherer
FIMM, FI

Sulev Koks
Tartu University
EE

→ *49 institutions – 9 countries*

Vaccines

Jan Langermans
BPRC, NL

Lucia Gabriele
ISS, IT

→ *15 institutions, (6 countries)*

Small Molecules

Mario Salmona
IRF Mario Negri Milan, IT

Alfredo Budillon
INT Pascale, Napels, IT

→ *26 institutions, (10 countries)*

Coordination & Support

Florence Bietrix

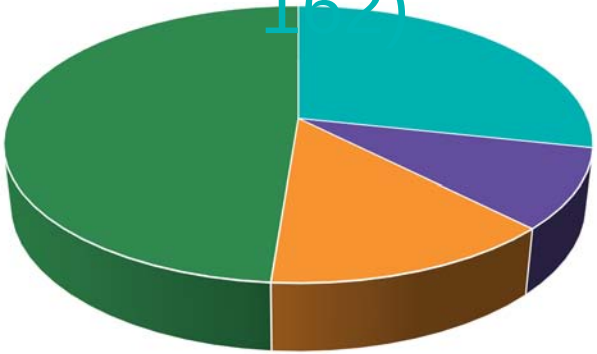
David Morrow

Martin de Kort

What do we do?

- User access to EATRIS research & expert services
  - Academic, industry and funders are users
- Develop new research tools
  - EATRIS Strategic Research & Innovation Agenda
- Education & Training
- Improve conditions for translation
  - New funding and collaboration models
  - EATRIS Quality initiative - reproducibility

EATRIS Client Portfolio 2014 - 2018 (n = 162)



- SME (46)
- Large Pharma (15)
- Funder (22)
- Academia (79)

EATRIS Quality Initiative

Imaging and Tracer Platform

- Europ. Soc. Mol. Imaging (ESMI) Study Group focused on the standardization of small animal imaging.
- Collaborating with EANM and EARL, jointly developing a 89Zr PET/CT accreditation program for the calibration of scanners to enable multi-site clinical imaging trials

Vaccines platform:

- Activities towards providing reference reagents in vaccine development (EURIPRED; a knowledge infrastructure across Poverty Related Diseases)

Small molecules platform:

- HTS Ring-testing (activity within “Translation together); phase 0 finalized; phase 1 involves 13 sites

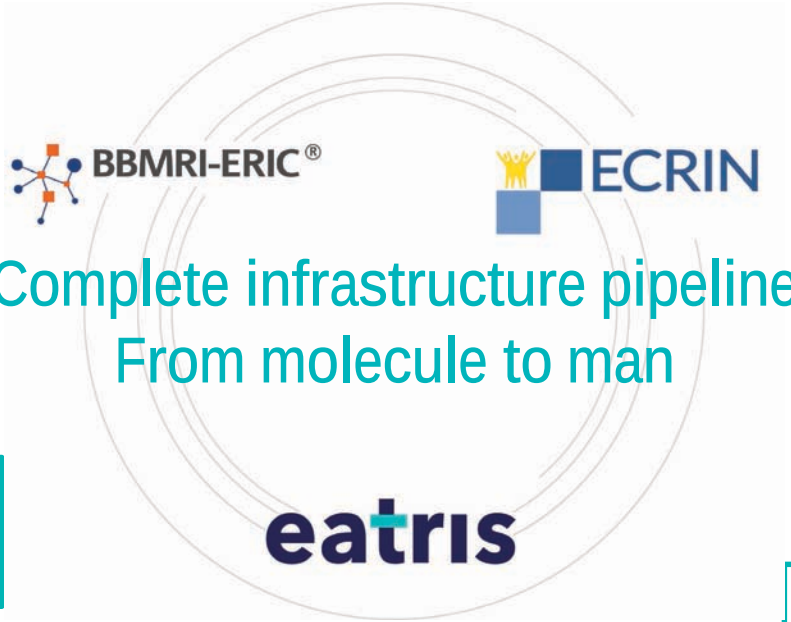
Biomarker platform:

- SEQC2 (Sequencing quality control)
- ctDNA-reference material: possible collaboration with US-consortium

Medical Research Infrastructure Alliance

Quality and reproducibility

Joint services



Education and Training

Sensitive patient data

Guidelines

Operational roles

What is the role of the Amsterdam **coordination unit**?

- Professionalising access
- Coordinating key projects (SRIA)
- Tackling systemic issues; i.e for EATRIS:
  - Reproducibility
  - Standardisation and harmonisation
  - Capacity utilisation - EU-wide long range planning?
  - Improving framework conditions for knowledge generation and innovation

Operational roles

What is the role of the **node/national consortium**?

- Coordinate national consortium & with C&S
- Providing access
- Executing intra- & extra- mural research
- Embedding in national eco-system
  - Collaborate with other infras, healthcare providers, NCAs etc.

National Coordination

- **Partner finding** for grant proposal preparation: Enhances Country participation in EATRIS-led grant applications
- **Community structuring** – building national community cohesion and collaboration through interaction with research and infrastructure partners (including other RIs) and institutions
- **Outreach and business development** – attending local industry partnering events, conferences, workshops to raise awareness of national and European EATRIS services
- **Supporting local community in EC grant preparation** Coordinating and leading input into projects, initiatives
- **Facilitating local events**, workshops and governance meetings for the European EATRIS community

For EATRIS to be successful

It takes commitment and effort from everyone

- **Be responsive** - read the Platform updates, read and answer mails that are relevant, attend meetings and teleconferences
- **Be proactive** - try to find colleagues that are relevant for matchmaking and other opportunities
- **Be creative** - the SRIA is a home for your great translational science - use it
- **Be communicative** - share the EATRIS message, disseminate in your institute and research community

Benefits of EATRIS membership

- Academic support - we offer a range of support services and resources to optimize your project (proposal)
- Industry partnering - active company client portfolio, support in reaching out to industry
- National infrastructure funding
- New communities - develop new collaborations across disciplines, sectors, countries and continents

Supporting your funding applications

Four levels of EATRIS C&S support

1. Consortium Building: to help with consortium building – identification of relevant institutions – list provided to PI, who contacts the institution(s)

2. Letter of support: for translational proposals and of high scientific quality

3. Provide services with EATRIS-ERIC as partner (i.e innovation management and industry partnering; Regulatory service; Translational Assessment Service…)

4. Leading role in proposal development for projects identified as flagship

Level 1: Consortium Building

- EATRIS can help you find the right European academic partner for your consortium thanks to a comprehensive database of the high-end capabilities and expertise of 90 top tier member institutions.

- This service is offered free of charge to any party (EATRIS members and non-members).

- If you are a member of the infrastructure, EATRIS can also support you to identify companies, charities or patient organisations for your consortium.

What are the criteria to benefit from EATRIS support for consortium building?

- The scope of the proposal idea must be translational;
- The PI is looking for areas of expertise and/or facilities that are crucial for project implementation.

Level 2: Letter of support

What are the criteria to obtain a letter of support from EATRIS?

- The scope of the proposal must be translational and of high scientific quality;
- The proposal must be in line with EATRIS mission: *“To support researchers in developing their biomedical discoveries into novel translational tools and interventions for better health outcomes for society”*;
- The consortium must be multidisciplinary with laboratory and clinical expertise represented; and when relevant, industry and/or patient organisations included as partners;
- The consortium must include institutions leading in their field and/or close collaborators of EATRIS (academic members or strategic partners);
- The proposal must explicitly commit to compliance with FAIR principles and include data management plan as a project’s deliverable.

Level 3: Joining as partner

- Proposals must meet criteria listed for level 2;
- EATRIS participation would clearly add value to the consortium and the proposal is consistent with EATRIS project portfolio;
- At least one EATRIS member institution participates in the proposal as partner or linked third party of EATRIS;
- The consortium is looking for “standard” type of services: e.g. regulatory expertise, HTA support, sustainability planning, industry partnering, access to training opportunities (provided by EATRIS Coordination Office in Amsterdam)

Level 4: Leading strategic projects

- From time to time, EATRIS will take a leading role in supporting the development and management of proposals coming from EATRIS member institutes, and identified as key potential contributions to the EATRIS Strategic Research and Innovation Agenda.

The proposal must fulfil the criteria mentioned for other levels and the following:

- The proposal idea is in line with EATRIS mission and with EATRIS Strategic Research and Innovation Agenda 2019-2022;
- The proposal is coordinated by an EATRIS institution;
- The proposal serves the research community by addressing systemic inefficiencies in medical research;
- The infrastructure can rely on strong expertise of many member institutions as project partners;
- The proposal is disruptive and will have a high impact on improving a translational pipeline, and therefore on the European Research Area.

Services provided by EATRIS as partner

Innovation Management & industry partnering

- Activities can include: design of the dissemination and exploitation plan of the project; definition and implementation of a monitoring plan to capture intellectual property protection needs in a timely fashion; identification of industry partnering opportunities for co-development and/or out-licensing; follow-up financing opportunities.

Translational optimisation

- Activities can include: monitoring of the project to ascertain a timely evaluation of the translational potential of the results generated during the project; full translational assessment to define follow-up validation route; early Health Technology Assessment (HTA) support.

Regulatory support

- Assessing the project's regulatory strategy and feasibility;
- Interacting with the relevant regulatory authorities;
- Answering any regulatory question arising during the project's lifetime;
- Ensuring the project fulfils all regulatory requirements

The EATRIS Platforms

EATRIS BIOMARKER PLATFORM

63 European advanced biomarker development centres

State-of-the-art technologies and expertise:

- Biobanks and associated medical data
- Liquid Biopsy
- Assay development and validation
- Clinical expertise
- Multi-centre clinical trials – prospective validation
- Handover to industry – early dialogue & partnering
- Regulatory and reimbursement

EATRIS BIOMARKER PLATFORM – Technology offering

Omics – technologies and bioinformatics:

- Genomics, next-gen DNA/RNA sequencing
- Proteomics, metabolomics…

Molecular pathology

- Multiplexed immunoassays and immunostaining of cells/tissues/TMAs
- Antibody libraries, antibody engineering and immunoassay development
- Automated images analysis and web microscopy

Targeted mass spectrometry

Multiparametric flow cytometry

COLLABORATING TOWARDS GOOD BIOMARKER PRACTICES

Biomarker Development Center

eatris
European infrastructure for translational medicine

BBMRI-ERIC
Biobanking and BioMolecular Resources Research Infrastructure

elixir

lygature
pioneering medicine. together.

COMMENT

Bridging the translational innovation gap through good biomarker practice

Alain J. van Gool[1], Florence Bietrix[2], Eric Caldenhoven[3], Kurt Zatloukal[4], Andreas Scherer[5], Jan-Eric Litton[6], Gerrit Meijer[7], Niklas Blomberg[8], Andy Smith[8], Barend Mons[9], Jaap Heringa[10], Wim-Jan Koot[3], Martin J. Smit[11], Marian Hajduch[12], Ton Rijnders[3] and Anton Ussi[2]

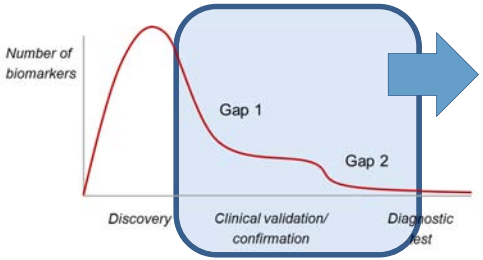
Few biomarkers progress from discovery to become validated tools or diagnostics. To bridge this gap, three European biomedical research infrastructures — EATRIS-ERIC (focused on translational medicine), BBMRI-ERIC (focused on biobanking) and ELIXIR (focused on data sharing) — are paving the way to developing and sharing best practices for biomarker validation.

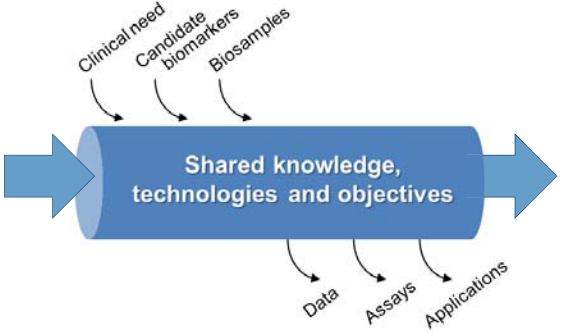
{{Nature Reviews Drug Discovery, Apr 2017}

clinical biomarkers

COST action CA16113
http://clinimark.eu

DEFRAGMENTING BIOMARKER VALIDATION CAPACITIES





Join forces among Europe's major academic infrastructures + industry to:

1. Establish "Good Biomarker Practice" guidelines

- on translational research, biomarker technologies, biobanking, data stewardship.

2. Efficiently execute high quality biomarker projects

- work together in clinical validation and development of probable biomarkers

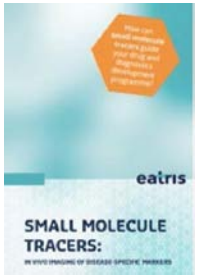
EATRIS IMAGING & TRACING PLATFORM

38 European advanced Translational Imaging centres

State-of-the-art technologies and expertise:

- Preclinical and clinical scanners
- PET, MRI (incl. 7T), US, optical
- Multimodal imaging (incl. PET/CT, PET/MRI)
- Nanomedicine formulation contrast agents
- Cyclotrons (all medical radioisotopes)
- Radiochemistry (GMP, >70 tracers)
- Preclinical, translational and clinical expertise
- Handover to industry – early dialogue & partnering

EATRIS IMAGING PLATFORM – Technology offering



- Access to new technologies and high-end academic infrastructure
- Early de-risking for drug candidates and therapeutic strategies
- Full development of imaging biomarkers, incl. data analysis
- Target engagement, patient stratification
- Tailored collaboration with pharma and SME clients
- Spur innovation in rare diseases and precision medicine

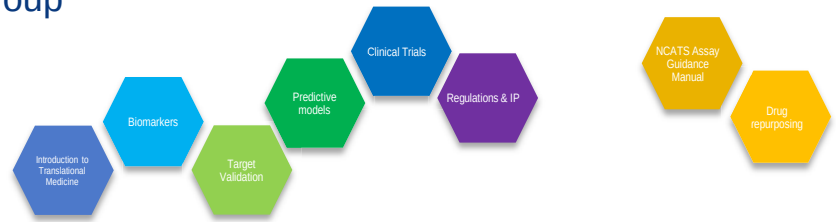
Educational activities - examples

- NEURATRIS (Paris) – Webinar series in Neuroimaging (Nov 2018):
  CEST-MRI for neurodegenerative diseases,
  Optical tools for brain cells,
  PET imaging to investigate neurodegenerative diseases
  Next edition, new topics in March 2019

- VHIR (Barcelona) – Translational Medicine course for PhDs and Postdocs (Ccomend project)
  Financial support by LaCaixa Foundation (next edition Nov 2019)

- University of Ljubljana - PPP Best Practice workshop (Dec 12-13, 2018; CORBEL project)

- TRANSLATION TOGETHER – E&T Working group
  expand E-learning, organize workshops,…



Multi-site Imaging: ^{89}Zr PET/CT Accreditation Program

Goal: Enabling multi-center trials with harmonized ^{89}Zr PET/CT imaging

Scope: Development of accreditation program with EANM/EARL

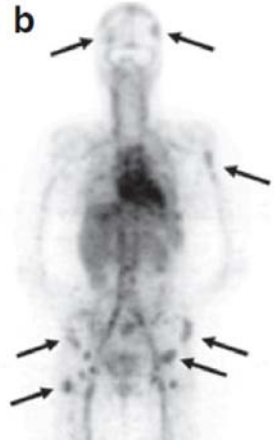
Preparation: Pilot phase (n=7) completed in 2017 (incl. EATRIS sites)

Potential scale: >150 eligible sites (already FDG accredited)

Immuno-PET quick start support: IMPD, SOPs, GMP compliance training

Current Status:

- Launch of accreditation program Jan 2019
- Operated by EANM/EARL

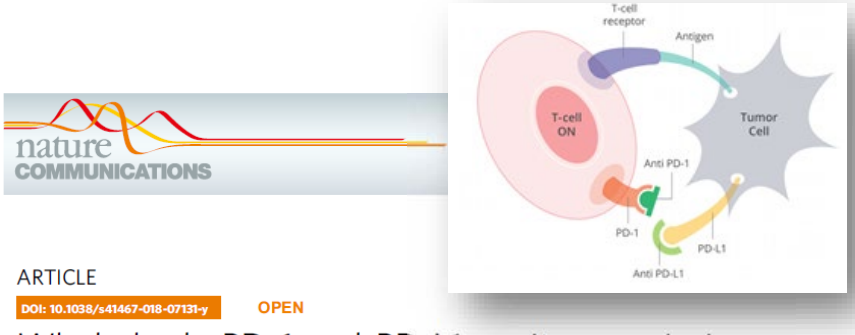


EARL 4 you

Accreditation

EANM

Imaging Supporting Pharma Drug Development



ARTICLE

DOI: 10.1038/s41467-018-07131-y OPEN

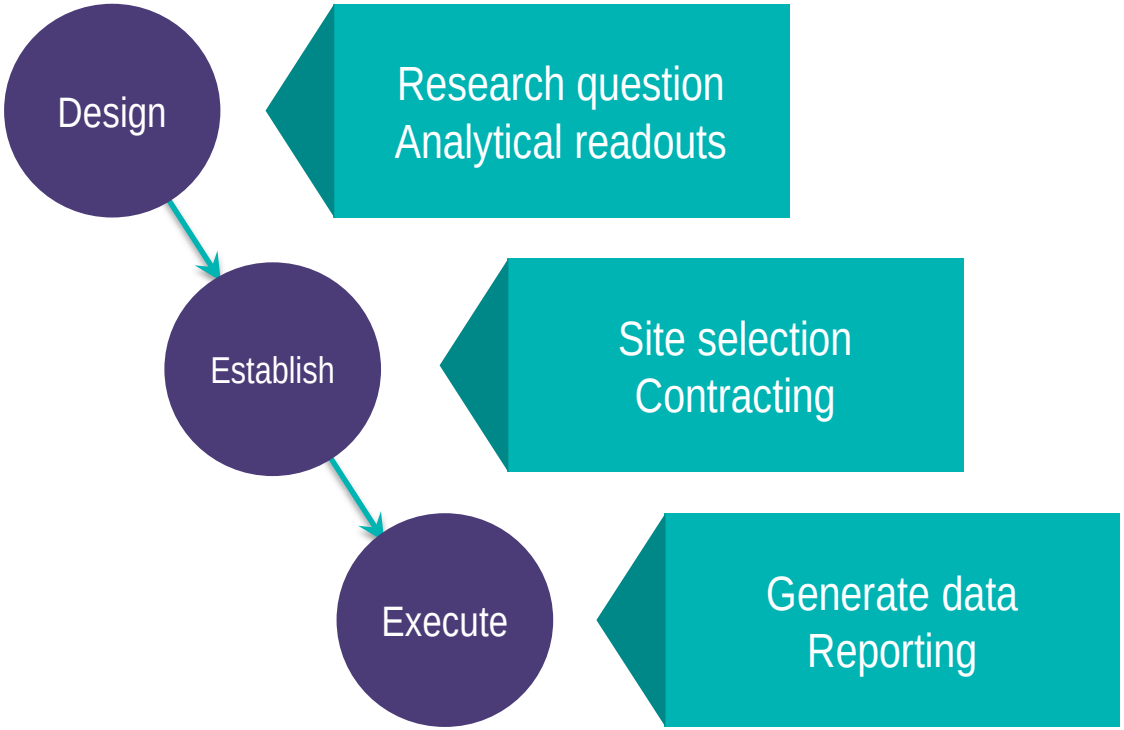
Whole body PD-1 and PD-L1 positron emission tomography in patients with non-small-cell lung cancer

A.N. Niemeijer[1], D. Leung[2], M.C. Huisman[3], I. Bahce[1], O.S. Hoekstra[3], G.A.M.S. van Dongen[3], R. Boellaard[3], S. Du[2], W. Hayes[2], R. Smith[2], A.D. Windhorst[3], N.H. Hendrikse[3], A. Poot[3], D.J. Vugts[3], E. Thunnissen[4], P. Morin[2], D. Lipovsek[2], D.J. Donnelly[2], S.J. Bonacorsi[2], L.M. Velasquez[2], T.D. de Gruijl[5], E.F. Smit[6] & A.J. de Langen[1,6]

Head-to-head comparison of [^{89}Zr]-nivolumab and [^{18}F]BMS986192 in same patients (n=13), against IHC.

Several EATRIS sites involved in industry collaborations

Industry research services



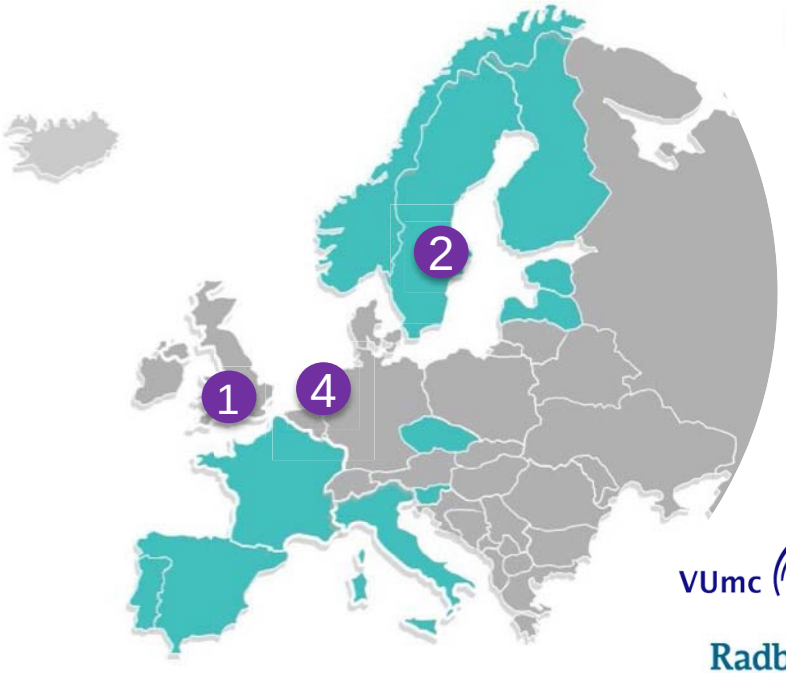
Various collaboration types supported

Type	Key success factors	Rate limiting factors
Single Service	Matching expertise	Finding the right partner Check: freedom to operate
Master Service	Robust platform Client orientation	Successful pilot
Collaborative	Trust Track record	Due diligence Audit(s)
Complex Collaborative	Aligning expectations early Project champion Single point of contact	Project complexity Lack of technical expertise Lack of PM capacity/experience
Collaboration Hub	Critical mass Long term commitment True collaborative spirit Facilitator/negotiator Administrator	Legal & operational design Slow decision making (private) Priorities, capacity planning (public)

(Based on EATRIS ERIC experience 2013-2018)

Incremental complexity

Public-Private Innovation Hub



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News

UNIQUE HUB COLLABORATION – IMAGING METHOD DEVELOPMENT IN INFLAMMATORY DISEASES

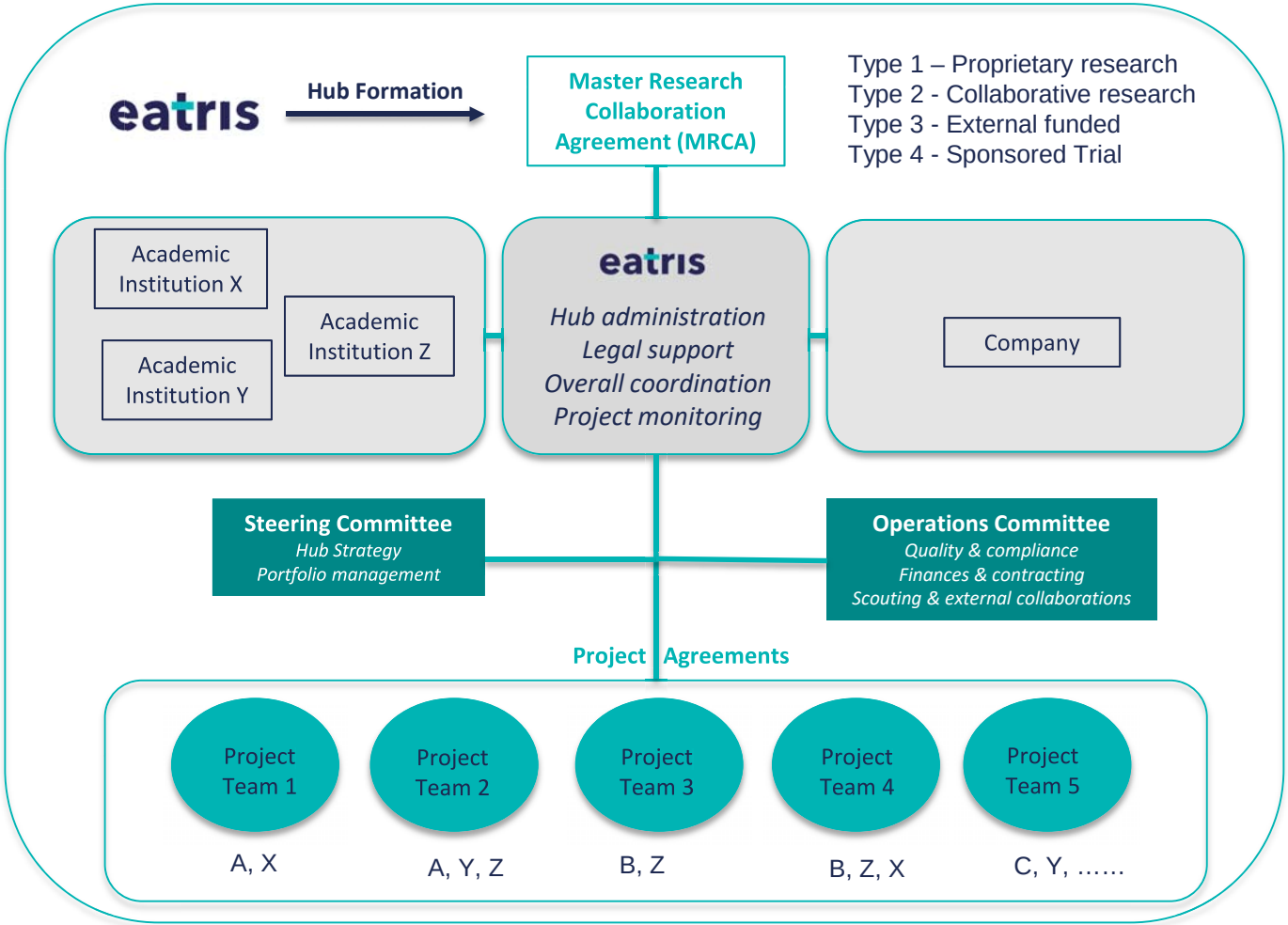
International multi-site collaboration hub will implement new clinical imaging tools and deliver several projects per year with enhanced speed and throughput.

Amsterdam, The Netherlands, June 4, 2018 – The European Infrastructure for Translational Medicine (EATRIS) has formed a collaboration with GlaxoSmithKline (GSK) to deliver a clinical and scientific expert network for the development and application of innovative imaging methods for inflammatory diseases.

Advanced imaging. The initiative is aimed at optimising existing imaging technologies for drug development and clinical translation of emerging probes.

While existing clinical imaging tools provide useful endpoints in clinical trials, they typically lack sufficient cellular and molecular information to fully understand drug response. Imaging has the potential to interrogate inflammatory cell populations, quantitatively in different tissues. This alliance aims to unlock this potential by delivering new clinical tools. Applying imaging in information-rich, small cohort studies can provide a high, immediate impact to enhance R&D productivity: developing our understanding of disease in the patient; enriching clinical trial cohorts; measuring therapeutic response.

The imaging hub aims to achieve these goals by (1) optimising existing magnetic resonance imaging (MRI) and positron emission tomography (PET) technology for drug development; and (2) translating emerging PET and optical cell-specific probes towards the clinic. The first three projects with a focus around immune cell specific imaging have now been initiated.


eatris
Hub Formation
Master Research Collaboration Agreement (MRCA)
Type 1 – Proprietary research
Type 2 - Collaborative research
Type 3 - External funded
Type 4 - Sponsored Trial
Academic Institution X
Academic Institution Z
Academic Institution Y
eatris
Hub administration
Legal support
Overall coordination
Project monitoring
Company
Steering Committee
Hub Strategy
Portfolio management
Operations Committee
Quality & compliance
Finances & contracting
Scouting & external collaborations
Project Agreements
Project Team 1
Project Team 2
Project Team 3
Project Team 4
Project Team 5
A, X
A, Y, Z
B, Z
B, Z, X
C, Y, ……

EATRIS SMALL MOLECULES PLATFORM

27 European Academic Drug Discovery centres

State-of-the-art technologies and expertise:

- Drug discovery platforms
  - HTS platforms (incl. X-ray / cellular and organoid screening)
  - Lead finding (MedChem/Pharmacology)
  - In vivo profiling
  - ADME profiling
- Peptide production (incl. GMP)
- Structural analysis (NMR, X-ray, LC/MS)
- (Re-)formulation labs

SMALL MOLECULES PLATFORM - Technology offering

Nanomedicines & Targeted Therapeutics for Precision Medicine

- Optimization of nanoparticle composition for clinical studies
- *In vitro* and *in vivo* safety / efficacy / profiling
- Compliant nanoparticle production

Advanced Screening

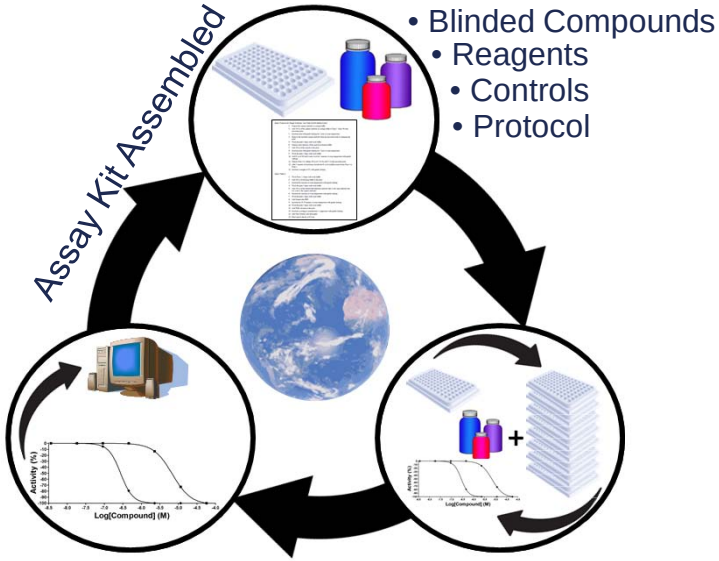
- PDX models for immune oncology
- Compounds collections of existing and novel drugs
- Organoid/ 3D cultures for tumor microenvironment screening
- Set up compliant *in vivo* models

Drug repurposing

- Chemosensitisers
- Drug synergisms for combination therapies
- Drug sensitivity screening / pharmacoresistance
- ODD designation application support

Quality Initiative: HTS screening

HTS ring-testing programme



Developed by *Translation Together*, a partnership of:

eatris

cdrd

MRC T

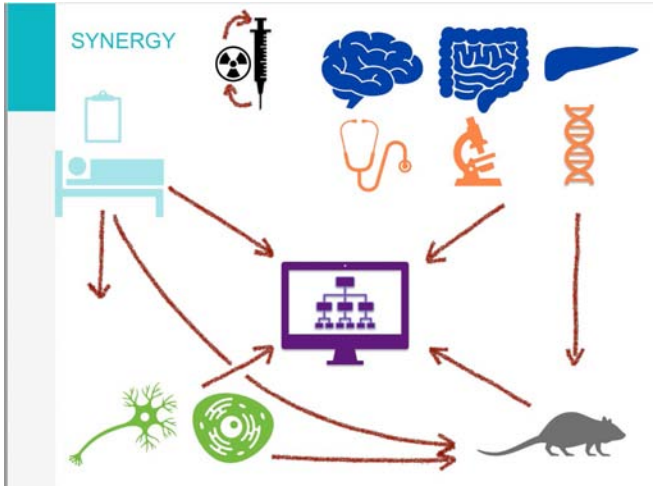
NIH National Center for Advancing Translational Sciences

THERAPEUTIC INNOVATION AUSTRALIA

AMED Japan Agency for Medical Research and Development

SYNERGY

H2020 specific challenge “SC1-BHC-02-2019:
Systems approaches for the discovery of combinatorial therapies for complex disorders”.



Rectal cancer
Pancreatic
Glioblastoma

HTS (X-ray/chemo), eHealth records, NGS, Machine Learning.

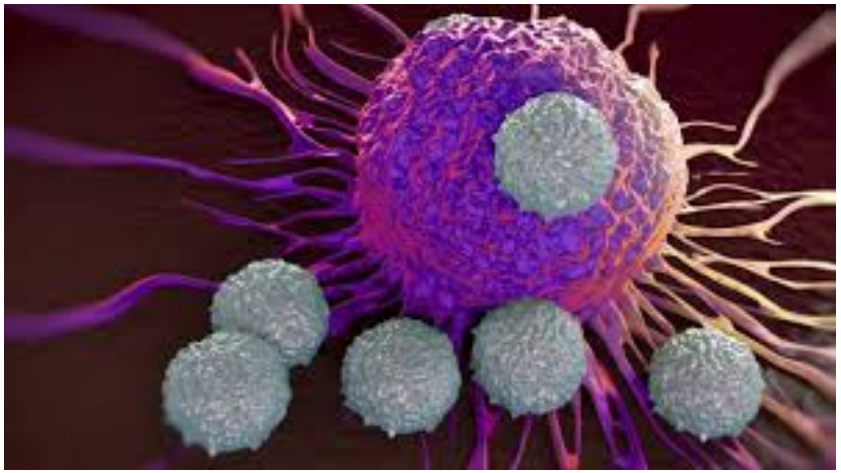
EATRIS ATMP PLATFORM

38 Advanced Therapy Research Centers

State-of-the-art technologies and expertise:

- Preclinical testing capabilities- preclinical animal models
- Genome editing and therapy
- Cell therapy and transplantation,
- Access to patients cohorts eligible for clinical trials with ATMPs
- Access to clinical facilities for carrying out Phase I/II/III clinical trials with ATMPs
- Support for trial design and execution under Good Clinical Practice
- Clinical testing capabilities, including routine as well as specialised clinical analyses, immune-monitoring, clinical imaging,
- Clinical tissue banking operations according to 2004/23/EU
- GMP Manufacturing
- Regulatory Support

What do we do as a Platform?



Supporting our Institutions in Developing Proposals

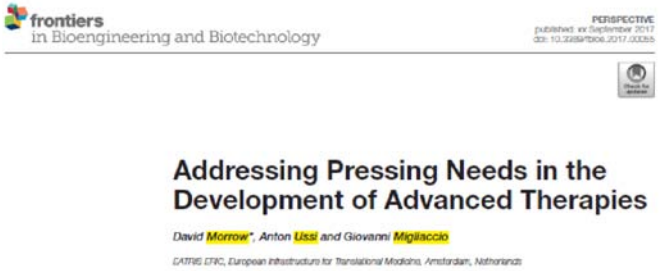
Example: SC1-BHC-07-2019: Regenerative medicine: from new insights to new applications (single-stage call; deadline: April 16 2019)

- Genome editing- CRISPR
- Gene therapy Expertise
- Transdifferentiation and *in vivo* reprogramming,
- cell therapy and Transplantation
- GMP Production of Cell and Gene Therapy Products
- Organoids
- Clinical Trial Facilities

EATRIS reviewed 8 applications – joined 2 as partner

Driving Funding Calls around key Challenges in ATMP Development

- The ATMP platform participated in an IMI consultation to identify bottlenecks in ATMP development. EATRIS formed a major part in the European Union (EU) wide **consultation** which resulted in the first **ATMP specific calls** which will be initiated in 2017/18 where EATRIS will participate in relevant consortia as they arrive.


frontiers in Bioengineering and Biotechnology

PERSPECTIVE

Addressing Pressing Needs in the Development of Advanced Therapies

David Morrow*, Anton Ussi and Giovanni Migliaccio

EATRIS ERIC, European Infrastructure for Translational Medicine, Amsterdam, Netherlands

- September 2017 EATRIS paper "**Addressing Pressing Needs in the development of advanced therapies"** accepted for publication. This papers promotes the need for an innovation group which involves the funder, industry, regulator and academic RIs to address systemic challenges in ATMP development. (**paper circulated at IMI for EATRIS involvement in funding proposal strategy)**

New Collaborations to Promote our Platform Resources and Expertise

- Conference/Workshop Development
- Mutual Marketing
- Business Development Activities
- EATRIS Expertise/Services Promotion at Conferences

Educational and Training Initiatives

Workshop D: Potency assays in advanced therapies and vaccines
Highlighting the strategy, pitfalls and regulatory pathway for the development of ATMPs and Vaccines

PROGRAMME

16:30 - 16:40	Introduction- Characterisation and Potency Assay strategy - Maria Cristina Galli & Lucia Gabriele (ISS, Italy)
16:40 - 17:00	Regulatory Guidance for Potency Assay Strategy Koen Brusselmans (Belgian Scientific Institute of Public Health) Marcos Timon (Spanish Medicine Authority) Ivana Haunerova (State Institute for Drug Control, Czech Republic)
17:00 - 17:30	Case Study Holoclar- Potency Assay Strategy for Market Approved ATMP - Graziella Pellegrini (Unimore)
17:30 - 18:15	Teams work on cases
18:15 - 19:15	Scientific Advice Meetings Panel of 5 regulators 1) Maria Cristina Galli (ISS) 2) Giovanni Migliaccio (EATRIS) 3) Marcos Timon (Spanish Medicine Authority) 4) Ivana Haunerova (State Institute for Drug Control) 5) Koen Brusselmans (Belgian Scientific Institute of Public Health)
19:15 - 19:30	Discussion and Wrap up

Collaboration with industry

Provide access to:

Scientific / medical expertise + technology in ATMP development

We identify academic partners that can offer specific expertise and technology to facilitate ATMP development including:

- Imaging & tracing capabilities
- Specific assays and animal models
- (rare) patient cohorts and samples
- Regulatory support
- GMP Manufacturing
- And much more…

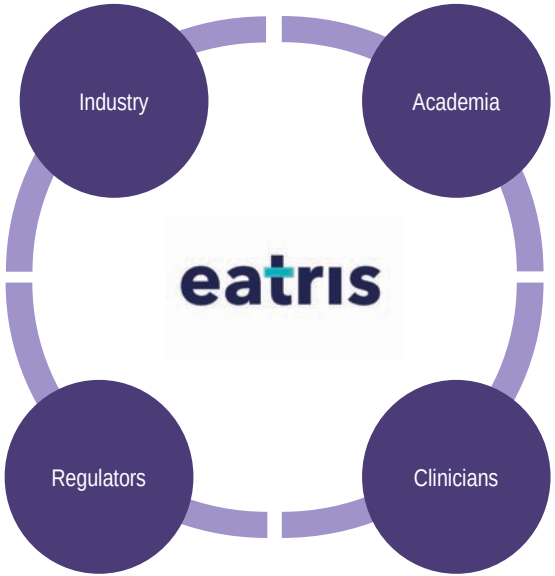
38 EATRIS ATMP Research Centers

Identifying Challenges in the ATMP Field

- Many **systemic bottlenecks in ATMP development** are due to weak/non-existent cross-sector cooperation.
    - Accessing **latest translational tools**, e.g.
    - Molecular imaging (cell tracking for CTs),
    - The right potency assays,
    - Assays addressing collateral effects of new therapies (e.g CRS from ACT)

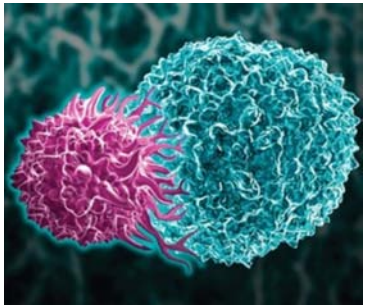
There exists a real need to develop and validate a quantitative, non-invasive, cell imaging platform for cell therapies

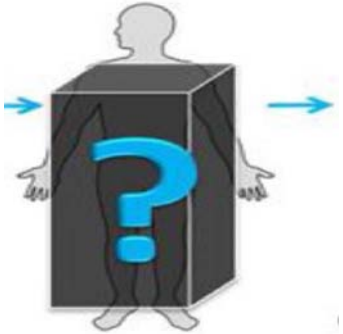
- EATRIS Flagship Project-



Cross-sectoral collaboration is a critical success factor

Lack of basic knowledge of CAR T cell behavior in vivo





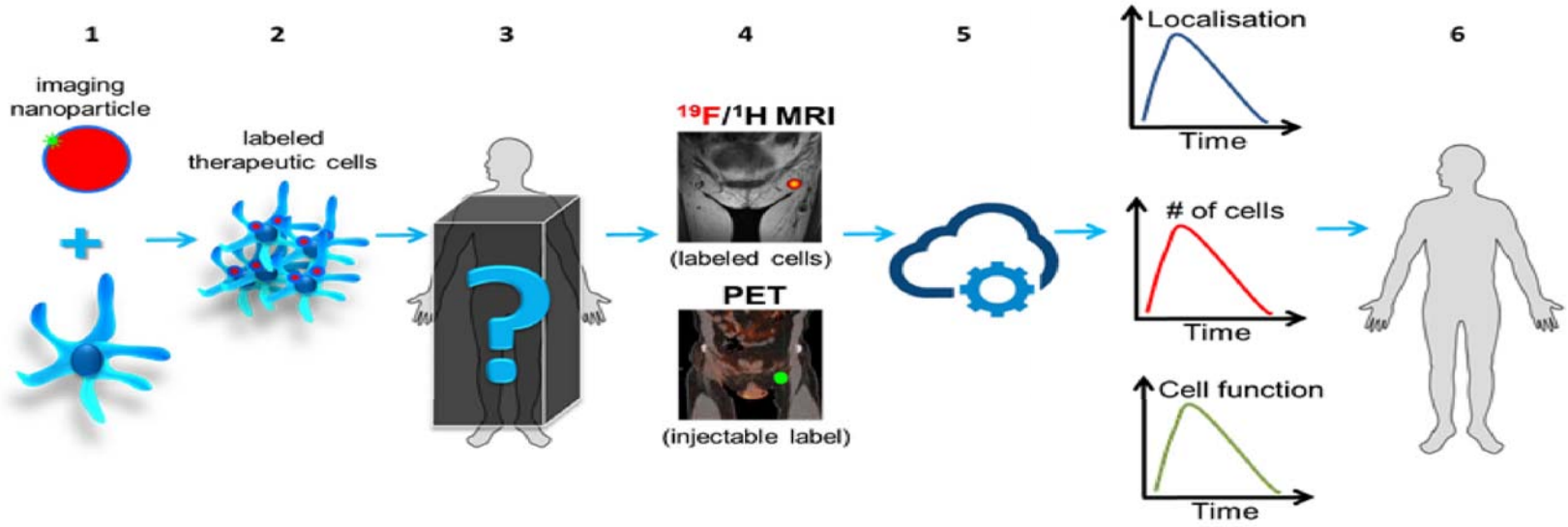
CAR T cell biodistribution?

Cell numbers at tumor?

Proliferation at tumor site?

Tumor infiltration?

How can we acquire a comprehensive picture, noninvasively, of what is happening in vivo with promising therapeutic cells?

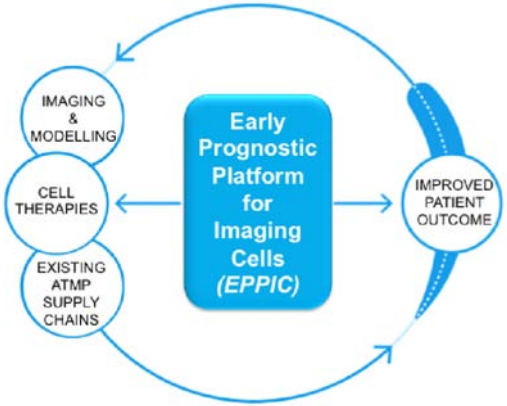


SC1-BHC-09-2018:Innovation platforms for advanced therapies of the future
-Level 4 Support-

What does the EPPIC Project want to deliver?

EPPIC foresees the close interaction of academic, clinical and industrial partners, and wishes to pursue a number of activities with diverse outcomes. It is envisaged that planned activities will deliver:

Objective:
Develop a broadly applicable platform, which incorporates noninvasive in vivo imaging and predictive modelling for the optimization of cell therapies, that is integrated into existing ATMP supply chains.



The Concept

The Platform

The Partners

Main Partners

Scientific Advisory Board

EATRIS Vaccine Platform

15 Participating Centers

State-of-the-art technologies and expertise:

- Antigen Production/Delivery Systems
- Preclinical Animal Models
- Vaccine Production Facilities
- Immunomodulation and Immunomonitoring Platforms for Vaccine Candidates
- Access to Patients Cohorts eligible for Clinical Trials with Vaccines
- Access to clinical facilities for carrying out Phase I/II/III Clinical Trials with Vaccines
- GMP Manufacturing
- Regulatory Support

EATRIS Vaccine Platform Initiatives

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IPROVE: The “Innovation Partnership for a Roadmap on Vaccines in Europe”, financed under the EU 7th Framework Programme in which EATRIS was one of the partners, was launched setting out a vision for vaccine rese-arch and innovation in Europe over the next 20 years. **(Now Published)**

EURIPRED is a collaborative infrastructure program, its objective the reinforcement of the knowledge infrastructure across diseases. Its aim is to speed the development of new tools (vaccines, drugs, microbicides) to combat tuberculosis, human immunodeficiency virus (HIV), malaria, hepatitis B virus (HBV) and hepatitis C virus (HCV). One of the key activities is providing reference reagents, services and trainings for free. **(Ends in Oct 2017- Reagents still available)**

TRANSVAC2 (2017-22) is a collaborative infrastructure project funded by the European Commission (EC), first under the 7th Framework Programme (FP7) and currently under Horizon 2020. The project is a joint effort of leading European groups in the field of vaccine development, and is coordinated by the European Vaccine Initiative (EVI). TRANSVAC is designed to accelerate vaccine development by enhancing European vaccine research and training, and increase sustainability of EC vaccine projects by implementing a permanent research infrastructure for early vaccine development. EATRIS makes up one of the 25 partners in this initiative which Kicked off in May 2017.

Offering Technology Platforms for New Vaccine Candidates.

- CD8 T-cell responses for vaccine candidates
- Mucosal immunity and vaccines
- Th1 and Th2 vaccine-induced immunity
- Long term immune memory
- Safety and tolerability-development of biomarkers of safety and protection from the bedside to the bench
- RNA vaccines
- Innovative clinical trials

Thank you for your attention and your engagement in Q&A

For further information

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antonussi@eatris.eu

Example Projects in the EATRIS Portfolio

Biomedical cluster project (until 2020)

"By harmonising **user access, unifying data management**, creating common ethical and legal services, and offering joint **innovation support** CORBEL will establish and support a new model for biological and medical research in Europe."

http://www.corbel-project.eu

CORBEL WP8 - fostering RI innovation potential

- Innovation office to be sustained after CORBEL
- Real time partnering & collaboration advice for RIs - open daily
- Template documents, guidelines and assistance with collaboration and knowledge sharing;
- Access to specialist knowledge in relation to business development and legal, regulatory or ethical aspects;

European Joint Programme in Rare Disease

Multi-stakeholder, patient-centred initiative to foster rare disease research from bench to bedside and back - 5 years, €108 million

EJP-RD goals include:

- structuring the connection with **European Reference Networks**;
- **research funding** (E-RARE ERA-NET);
- promoting improved **research methodologies** for rare disease research;
- More **effective translation and professional mentoring**;
- ensuring **patient involvement** in all steps of the research pathway;
- **FAIR** principles (Findable, Accessible, Interoperable, Re-usable);

EATRIS leads Pillar 4 (translation & clinical) & Sustainability

Early HTA & Feasibility Assessment

EATRIS developed early HTA framework for ZonMw

- For Translationeel Adult Stamcelonderzoek programme 2018
- Uses EUNetHTA 9 point model plus EATRIS principles

Working with Reuma Nederland and ZonMw since 2014

- Assessing translational feasibility of translational research projects
  - Unmet medical need
  - IP status
  - Technological novelty (competitive landscape)
  - Regulatory pathway

EATRIS 2013 - 2018

Establishing pan-EU access to high quality infrastructure

GSK - Immuno inflammation Imaging Hub

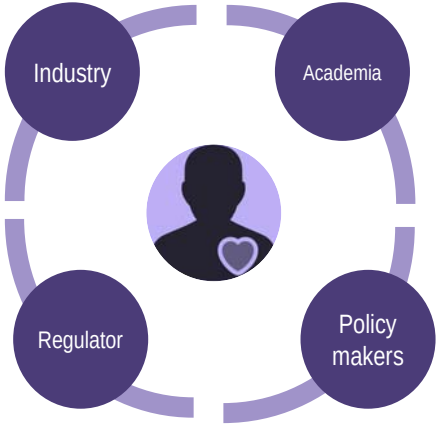
- Next generation public-private collaboration
- Translating new molecular inflammation imaging targets and probes to humans

Press Release, June 2018

EATRIS 2013 - 2018

Enabling multi-sector innovation

- Identify systemic bottlenecks
- Develop new ways to fund/collaborate
- Work directly with charities/funders
- Work directly with regulators



ECADE
Early Cancer Detection Europe

Bring together expertise to help select and design validation of biomarker study for early cancer detection

UniSR
UNIVERSITÀ VITA-SALUTE SAN RAFFAELE

ZonMw

Designed early HTA framework
For €8mn call financed by Min. Health
For more patient-centric, affordable innovation

EATRIS 2013 - 2018

Enabling multi-sector innovation: Human + Social venture capital, 21 charities and EATRIS-ERIC collaborating for better patient outcomes

human+

1- All NL health charities & ZonMw can apply for VC co-funding (33%)

2- EATRIS performs feasibility assessment

3- Human+ Investment Board decides on funding

4- EATRIS supports execution as needed

EATRIS 2013 - 2018

Working with global with peers – Translation Together

translation together

CDRD THE CENTRE FOR DRUG RESEARCH & DEVELOPMENT

lifeArc

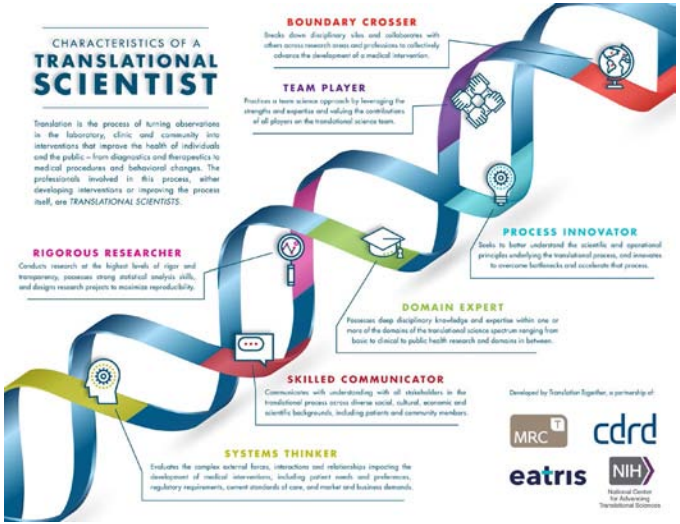
NIH National Center for Advancing Translational Sciences

THERAPEUTIC INNOVATION AUSTRALIA

eatris

AMED

国立研究開発法人 日本医療研究開発機構
Japan Agency for Medical Research and Development



Objectives

01 >
Coordinate and develop programs and resources for educating and training the next generation of translational scientists and other key stakeholders.

02 >
Advocate for a broad understanding of and appreciation for translation and translational science among diverse stakeholders.

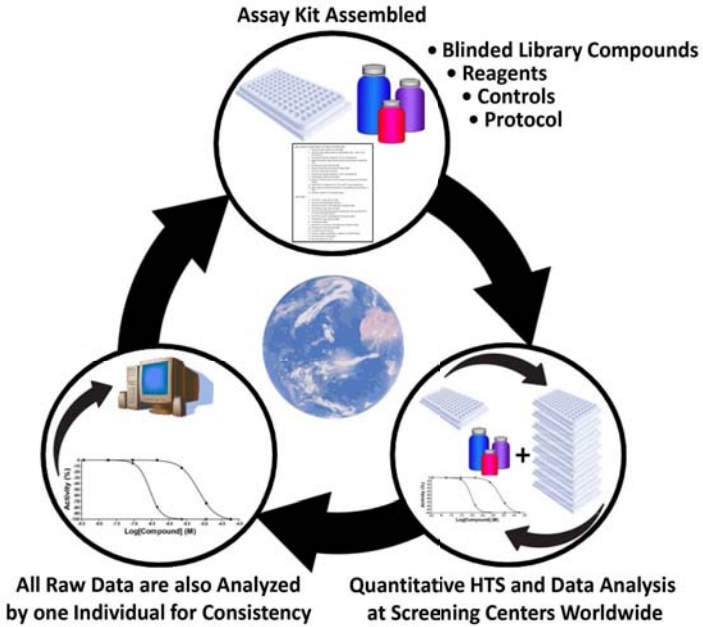
03 >
Assist investigators in the conduct of translation and translational science by connecting them to resources, tools, technologies, and expertise.

04
Conduct collaborative research projects to remove systemic barriers and catalyze translation.

EATRIS 2013 - 2018

Working with global with peers – EATRIS Quality Initiative

HTS Ring Testing



- **Explore reproducibility of HTS experiments** - identify sources of variation among participating centers:
  - Blinded library of Pharmacologically Active Compounds luciferase biochemical assays with Photinus pyralis and Renilla reniformis
  - All experiments are performed with identical reagents and protocols supplied by NCATS
  - All data analyses performed at NCATS as well as each participant individually